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Case Report

Primary Ewing's Sarcoma of the Occiput: A Case Report

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Abstract

Introduction and importance: Ewing's sarcoma is a malignant small, round cell tumor arising in the bones and affecting the younger population. This tumor mostly occurs in the long bones of extremities. Primary cranial Ewing's sarcoma is uncommon with primary Ewing's sarcoma of the occipital bone being very rare which can sometimes cause diagnostic dilemmas.

Case presentation: A six-year-old male presented to our neurosurgery outpatient department with the chief complaint of rapidly progressive, painless swelling over the occipital region for thirty days with headache localized to the occipital region. There were no symptoms or signs suggestive of neurological deficits or metastasis. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of the brain revealed a mass in the occipital region with intra and extracranial components with features pertaining to malignant etiology. Histopathology of resected specimens with immunochemistry was consistent with Ewing's sarcoma. Patient is scheduled for adjuvant chemotherapy.

Clinical discussion: Ewing's sarcoma is a highly malignant bone tumor of young population that commonly affects the diaphyses of the long bones, pelvis, rib, vertebrae, jaw and cranium. Its occurrence on skull bone is rare and on occipital bone is scarcely mentioned in the literature. Earlier symptoms may include occipital headache, vomiting, scalp swelling or papilledema. CT and MRI brain are suggestive and histopathology with immunochemistry is diagnostic. Primary Ewing's sarcoma of skull bones has good prognosis and can be managed with surgery and radio ± chemotherapy.

Conclusion: Rarely, Ewing's sarcoma originates in the skull bone, and very rarely originates in the occipital bone of skull. Histopathology and immunochemistry will differentiate it from osteosarcoma/lymphoma/leukemia/hemangioma of the skull/giant cell tumor/neuroblastoma/rhandomyosarcoma. When early identification is done, it can be managed through resection and adjuvant chemotherapy.

Keywords: Ewing's sarcoma; Occiput; Histopathology; Adjuvant chemotherapy

Introduction

Ewing's sarcoma is an aggressive, malignant, small, round cell tumor arising from bone and primarily affects children and adolescents. It is considered the second most common pediatric primary bone tumor, accounting for 6 to 9% of malignant bone neoplasms in children. It affects mainly the long bones and pelvis and less often affects the skull (i.e., maxilla, frontal, parietal, ethmoid, temporal bones) [1]. Primary cranial involvement accounts for approximately 1% of Ewing's sarcoma cases, with a primary occipital bone tumor being considered very rare [2].

Ninety percent of these cases occur in the first or second decade of life with a slight male predominance, with a ratio of 1.4:1 [3].

Ewing's sarcoma was first described by James Ewing as "endothelioma of the bone". In 2002, The World Health Organization classified Ewing's sarcoma with Primitive Neuroectodermal Tumor (PNET) as a single pathological entity [4]. Therefore, the term Ewing's sarcoma/PNET family of tumors is currently employed.

In this report, a rare case of primary occipital Ewing's sarcoma has been described with the significant clinical history, examination findings, diagnostic modalities and management.

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Case Presentation

A six-year-old male presented to our Neurosurgery Out-Patient Department with the chief complaint of rapidly progressive, painless swelling of the occipital region, for 30 days with a history of localized headache in the occipital region for the same duration. However, there was no history of fever, vomiting, abnormal body movement, loss of consciousness, dizziness, difficulty in speech, weakness of limbs, gait abnormalities, weight loss and bowel or bladder abnormalities. The child didn't not give a history of altered or decreased vision. There was no history of bone pain or fractures, chest pain, shortness of breath, hemoptysis or yellowish discolouration of the body. On examination, the child was afebrile and his vital parameters were within normal limits. There was no associated cervical lymphadenopathy. Examination of the occiput revealed a single, hard, non-fluctuating, non pulsatile, non-tender and non-discharging oval swelling with ill-defined edge measuring approximately 8 cm × 7 cm which was fixed to the scalp and underlying bone (Figure 1). The overlying skin was intact and there were no signs of inflammation. Neurological examination of the patient was unremarkable, without any focal neurological deficits. Other systemic examinations were within their normal limits.

On hematological investigations, total leucocytes count was 12,200/cmm, hemoglobin of 11.8 gm/dl and platelets of 4,22,000/cmm. Renal and liver function parameters were within their normal range. CT scan of the head was done which showed 'lytic sclerotic bony lesion with extensive soft tissue component in the occipital region with extension into intracranial as well as extracranial soft tissue suggesting features of malignant pathology (Figure 2) and non-

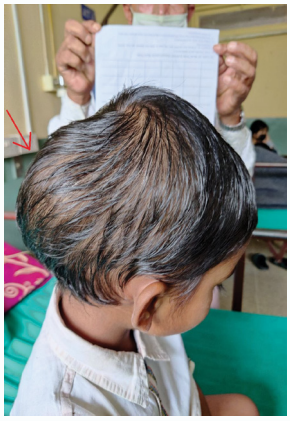

Figure 1: Large occipital swelling in a 6-year-old male at the time of presentation to our center.

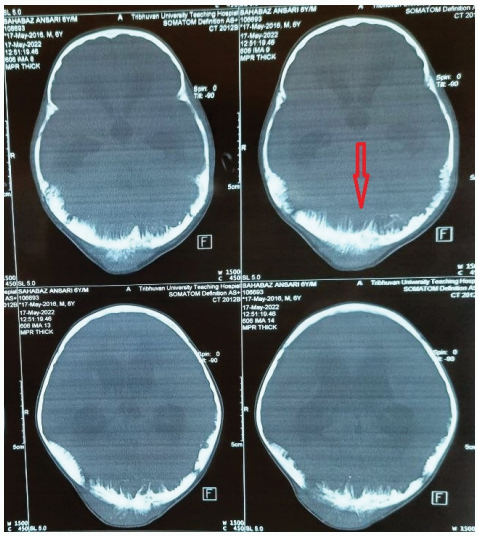

Figure 2: Plain CT head showing lytic sclerotic bony lesion with extensive soft tissue component in the occipital region with extension into intracranial as well as extracranial soft tissue.

communicating hydrocephalus (Figure 3). Further; MRI was done which showed 'mass of size approximately 10.5 (cc)*7.2 (AP)*9.3(T) cm in occipital region with intra and extracranial components compressing and distorting the posterior cranial fossa structures'. Mass was obliterating the 4th ventricle with markedly dilated lateral and 3rd ventricles with T2 periventricular hyperintensity. Rest of the brain showed normal morphology with normal parenchymal signal intensity (Figure 4 and 5). MR venogram showed encasement of the right transverse sigmoid sinus with the abutment of superior sagittal and left transverse sinus (Figure 6). Based on the characteristics observed on the imaging studies, potential diagnosis of Ewing's sarcoma/osteosarcoma/leukemia was made. Bone marrow aspiration and biopsy was done which was negative for malignancy. Primary screening of long bones of extremities, pelvis, vertebrae and ribs, and lung were done to look for primary or secondaries through X-ray which were negative. Screening of cervical spine through MRI revealed no abnormality (Figure 5). Ultrasonography of the abdomen was negative for liver metastasis. There were no other possible signs of distant metastasis. After counseling the child's family, a biopsy with possible resection of the lesion was planned using occipital craniectomy with tumor excision followed by cranioplasty. The patient underwent a gross total surgical resection of the tumor with operative findings revealing highly vascular mass arising from occipital bone with dense adherence to dura with areas of necrosis, bleeding and thrombosis. Craniectomy was done including adjacent normal bone, and tumor excised all around. Tumor adherent to adjacent dura was coagulated and scrapped off. Acrylic flap was prepared and applied, and fixed with MRI compatible Titanium plates and screws. Intraoperative period was unremarkable. Final histopathology revealed a partially circumscribed tumor composed of tumor cells with a high nucleo-cytoplasmic ratio with a round to oval nuclei and scant cytoplasm along with areas of hemorrhage and necrosis, tumor cells also infiltrating bone along with marrow cavity. In immunohistochemistry; CD 99 was positive with negative status for desmin, myogenin and CD 45, findings consistent with Ewing sarcoma; with this a final diagnosis of Ewing's sarcoma of occiput was made. The postoperative course was uneventful with one day of Intensive Care Unit (ICU) stay. Patient is planned for adjuvant chemotherapy with vincristine, doxorubicin, cyclophosphamide alternate with ifosfamide and etoposide for 6 months at 3-week cycles.

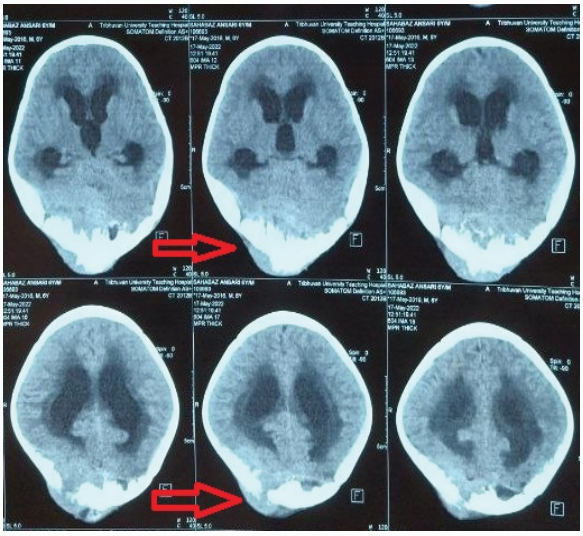

Figure 3: Plain CT head showing mass in the occipital region and non-communicating hydrocephalus.

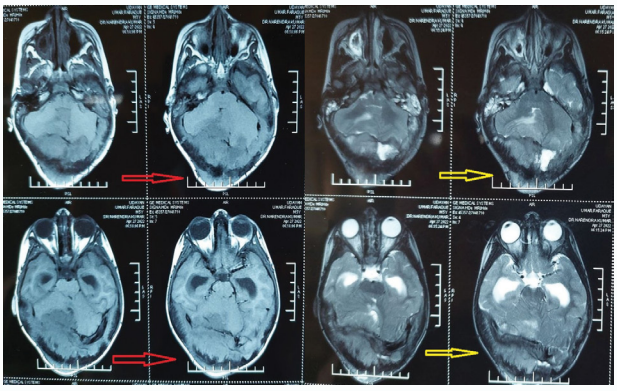

Figure 4: MRI of brain axial T1 and T2 weighted images showing large irregular extra-axial mass lesions seen posteriorly in the occipital region as well as mildly extending into the parieto-temporal region. The lesion is irregular and lobulated with involvement of adjacent calvarium and intermediate to hypointense on T1 (red arrow) and heterogeneously intermediate to hyperintense on T2 (yellow arrow).

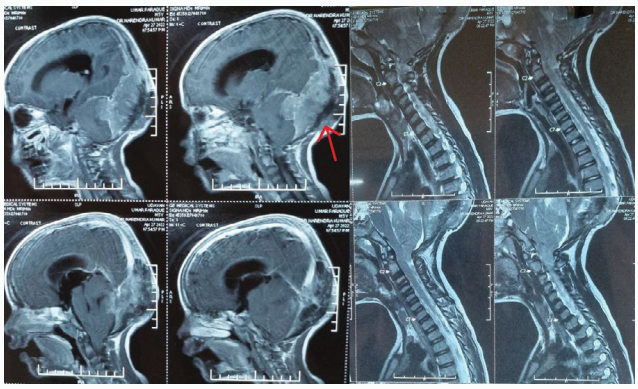

Figure 5: MRI T1 Sagittal section of brain showing mass in the occipital region with both intra and extracranial components. Screening of cervical spine reveals no obvious significant abnormality.

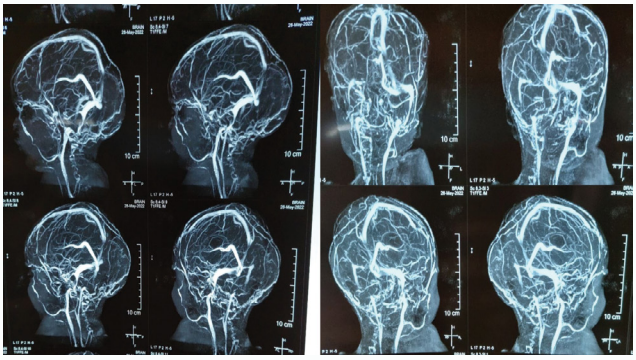

Figure 6: Magnetic Resonance venogram of intracranial veins showing mass in the occipital region with intra and extracranial components with encasement of the right transverse sigmoid sinus. Abutment of the superior sagittal and left transverse sinus.

Discussion

Ewing's sarcoma is a highly malignant bone tumor that commonly affects the diaphyses of the long bones, pelvis, rib, vertebrae, jaw and cranium [5]. Metastatic Ewing's sarcoma to skull bones is seen frequently, but primary Ewing's sarcoma of the skull bone is rarely encountered in neurosurgical practice [6].

Ewing's sarcoma that affects the skull accounts for only 1% to 6% of total cases and usually develops in patients younger than 20 years [7], Primary Ewing's sarcoma of the skull typically respects dural planes and often presents as an expansile mass typically affecting the frontal and parietal bones, as well as the temporal bones [1], causing symptoms of increased intracranial pressure. The most frequent sites in primary cranial Ewing's sarcoma are temporal followed by frontal [5,8] Ewing's sarcoma usually follows a highly malignant course due to early dissemination to the lungs and other bones; however, early metastasis is infrequent in cranial Ewing's sarcoma. Therefore cranial Ewing's sarcoma carries a better prognosis compared to that of other body sites [9].

The initial clinical features of primary ewing's sarcoma involving the cranial bones are generally atypical, headache being the most common symptom and papilledema the most common sign. Most patients present with gradually increasing scalp swelling, headache and vomiting.

Plain radiographs of the skull may show signs of new bone formation in the form of onion peel appearance, resulting from new bone formation in parallel layers, with mottling and overlying bone erosion. On the CT scan, these are extradural tumors that are iso-to hyperdense and show enhancement on contrast administration [5]. With the development of diagnostic radiological techniques such as Magnetic Resonance Imaging (MRI), extra skeletal masses can be depicted clearly and the tumor area can be accurately evaluated [10].

Cranial CT or radiography of Ewing's sarcoma reveals lytic lesions with poor margination and often a `moth-eaten' appearance. The `onion-skin' appearance due to the periosteal reaction is more common in the long bones than in the spine. MRI shows the tumor as hypointense compared to normal bone on T1-weighted images and hypointense to hyperintense on T2-weighted images. Moderate, uniform enhancement is seen after administration of intravenous contrast medium [11].

Radiologically, Ewing's sarcoma shows bone destruction in a permeative pattern that may be accompanied with large soft tissue involvement, indicative of a highly aggressive tumor. Tumors involving the skull with adjacent soft tissue have comprehensive differential diagnoses, which includes metastatic tumors such as neuroblastoma, lymphoma, and rhabdomyosarcoma and primary tumors such as meningiosarcoma and sarcomatous malignant lesions. Radiologically, neuroblastomas usually have hair-on-end periosteal appearance, osteolytic lesions, and separation of sutures [12]. Secondary skull lymphomas present as lesions extending to both the subcutaneous and epidural spaces, with meningeal penetration [13]. Rhabdomyosarcoma tumors tend to be isointense to muscle on T1-weighted images and high in intensity on T2-weighted images, with the orbit being the primary site in 90% of cases [14]. However, a case was reported with rhabdomyosarcoma in the occiput with gray color, compressing the brain tissue and thereby mimicking Ewing's sarcoma with no signs of calcification on imaging [15]. Moreover, primary meningeal sarcoma tumors show cystic structures within the masses, heterogeneity on contrast enhancement, and connections to the meninges [15,16].

However, biopsy of the tumor remains the best mode for obtaining a definitive diagnosis. If representativeness of the biopsy is an issue, a frozen section examination can be performed for adequacy. But now translocation analyses are being used not only for the diagnosis and classification of small round cell tumors, but also to ascertain their prognostic significance, detect micrometastasis, and monitor minimal residual disease, with potential for targeted therapy [10].

Histopathologic features of Ewing's sarcoma show monotonous sheets of monomorphic round cells with scant cytoplasm, round nuclei, and inconspicuous nucleoli [17,18]. Molecular genetic analysis for chromosomal translocation t(11:22)(q24; q12) is pathognomonic [19]. Overexpression of CD99, a transmembrane protein encoded by the *MIC-2* gene, is another helpful adjunct [20,8]. Rhabdomyosarcoma, which is high on the differential as the most common skull base sarcoma in the pediatric population, is also a small, round, blue cell tumor that can be easily confused with Ewing sarcoma. In both cases, initial biopsy of an infiltrating skull base tumor is usually the most appropriate intervention because these tumors typically respond quickly and dramatically to chemotherapy. Immunohistochemical analysis of Ewing's sarcomas reveals expression of vimentin and CD99, with characteristic perinuclear staining [20,21]. Antibody against FLI1, which is centered in the nucleus of the tumor cells, has been shown to be specific for EFT [22]. Depending on the degree of

neuroectodermal differentiation, the tumor cells may also express Neuron-Specific Enolase (NSE), synaptophysin, and S-100 protein [10]. CD99 may also be expressed in lymphoblastic lymphoma and leukemia, but it is negative in neuroblastoma. Thus the differential diagnosis of intracranial small-round-cell-tumors should include neuroblastoma, rhabdomyosarcoma, lymphoma and leukemia. In our reported case, neuroblastoma was excluded since CD99 was positive. Lymphoblastic lymphoma and leukemia were excluded since leukocyte common antigen (CD45) was negative. Rhabdomyosarcoma was excluded since desmin was negative.

Preoperatively, the tumor appears as a brownish vascular mass with invasion of muscle externally and dura internally. Brain invasion is rare, and may be mistaken for a glioma if present. Radical surgery has been advocated, but these tumors are sensitive to radio- and chemotherapy, so a less aggressive approach should be considered [2,23-27,11].

Treatment options for Ewing's sarcoma include induction chemotherapy, local control, and adjuvant chemotherapy. Chemotherapy, using a multimodal therapeutic regimen, has greatly increased survival from less than 10% to more than 50% [6]. The current chemotherapy protocols used to treat ES include various combinations of the following six drugs: Doxorubicin (DOX), Cyclophosphamide (CPM), Vincristine (VCR), Actinomycin-D (ACT-D), Ifosfamide (IFO), and Etoposide (ETO) [28]. Before the introduction of chemotherapy, most patients died of metastatic disease within 2 years. Options for local control include surgical excision and radiation. Radiation is the primary local control modality when tumors are difficult to access or when surgical excision would lead to morbidity. In contrast with patients with Ewing's sarcoma affecting the pelvis or lower body, patients with cranial lesions often undergo urgent surgical treatment because of elevated intracranial pressure and impending neurological deficits; consequently, induction radiation or chemotherapy is not commonly used. Tumors arising from the calvarium may be amenable to complete surgical resection. In our case surgical excision was possible because of the size of the tumor, its anatomical location without evidence of metastasis. Better understanding of how local control can be achieved has helped to improve the oncological outcomes of ES. Female gender, the absence of systemic symptoms and metastasis at diagnosis, long duration of symptoms (more than six months), and peripheral tumor location are indicators of favorable prognosis [29]. Various factors indicate a good outcome for patients with cranial Ewing's sarcoma: Duration of symptoms for a period of longer than 6 months; absence of fever or systemic symptoms; peripheral localization of the tumor and absence of metastases; initial lactate dehydrogenase levels of less than 170 IU/l; leukocyte count of less than 7000/dl; and lymphocyte count of less than 2000/dl [2]. Although the survival rate of ES patients has improved, their prognosis remains unsatisfactory, and the treatment of ES is still challenging to the medical teams involved, which include orthopedic surgeons, pediatric oncologists and radiotherapists.

Conclusion

Although primary Ewing's sarcoma of the cranium is a malignant bone tumor, it is associated with a good prognosis when treated with radical surgery, aggressive multidrug chemotherapy, and radiotherapy. The short average duration of symptoms (2 months) in our case suggested rapid growth of the tumors. Primary cranial Ewing's sarcoma should be considered in the differential diagnosis of pediatric extra-axial dural based posterior fossa masses, particularly when associated with involvement of the adjacent bone. To improve prognosis, Ewing's sarcoma of the Central Nervous System should have screening of the entire neural axis for early detection.

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